CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE
SUMMARY OF TOXICOLOGICAL DATA
MEDICAL TOXICOLOGY BRANCH

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DEMETON (SYSTOX)

SB 950-112, Tolerance #105

July 15, 1986

I. DATA GAP STATUS

Chronic rat: Data gap, inadequate study, no adverse effect indicated

Chronic dog: Data gap, no study

Onco rat: Data gap, no study

Onco mouse: Data gap, no study

Repro rat: Data gap, no study

Terato mouse: Data gap, inadequate study, no adverse effect demonstrated

Terato second mammalian species: Data gap, no study

Gene mutation: Data gap, no study

Chromosome: Data gap, no study

DNA damage: Data gap, no study

Neurotox: Data gap, inadequate studies, no adverse effect demonstrated

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Note, Toxicology one-liners are attached
** indicates acceptable study
Bold face indicates possible adverse effect
Demeton.sum 06b sb 112

II. GENERAL COMMENTS

1. Demeton (Systox) is a mixture of O,O-diethyl O-(2-(ethylthio)ethyl) phosphorothioate and O,O-diethyl S-(2-(ethylthio)ethyl) phosphorothioate. This is important because the former is far more toxic than the latter and because the proportion varies in different pesticide products. See "Toxicity and Mechanism of Action of Some Metabolites of Systox" Record #959237, Document #105-004, Tab #19326 and "Toxicity and Mechanism of Action of Systox" Record #959215, Document #105-008, Tab #587.
2. There are human feeding studies for demeton. See "Pharmacology and Toxicology Feeding Studies - Men and Dogs", Document #105-005; and "Toxicity of parathion, systox, octamethyl pyrophosphoramide, and methyl parathion in man", Record #959252, Document #105-004, Tab #25535.

III. TOXICOLOGY ONE-LINERS

CHRONIC, RAT

006 959227 (Undated, U. Miami; 8/4/53, Serum Research Institute, Surrey) JW 4/8/85; Re-review BKD 7/15/86. One liner: Tabular summary of 006 959210 and 006 959251, neither of which is CHRONIC since dosing was for 90 days in 006 959210 and 11 or 16 weeks in 006 959251. Data gap.

042 26864 (14/11/51, Albany Medical College) BKD 7/17/86. One liner: Progress Report predating 006 959227, 006 959210, and 006 959251.

008 959215 (4/55, Albany Medical College and University of Miami) BKD 7/17/86. One liner: Publication in A.M.A. Archives of Industrial Health, identical with 006 959210.

CHRONIC, DOG

057 040996 (1/20/84, Bayer AG). VVW and BKD 7/14/86. One liner: Historical control data on body weights of beagle dogs from 30 chronic toxicity studies, 1973-83, from 6 European breeders, at the Bayer AG Institute of Toxicology. This record could serve as historical control data for a number of dog studies. Some compounds are referenced by code numbers. If these were provided, diuron and/or other test substances could also incorporate these data with their studies. No full studies have been submitted yet on chronic dog, demeton.

ONCOGENICITY, RAT

057 040994 (1983, Bayer AG). VVW and BKD 7/14/86. One liner: Historical control data from 21 chronic toxicity rat studies, Bayer AG Inst. of Tox. from 1975 to 1983, report 88769. This may provide useful information for an oncogenicity study submission. No rat oncogenicity study is on file.

ONCOGENICITY, MOUSE

057 040993 (11/80, Mobay AgChem and various contract laboratories). VVW and BKD 7/14/86. One liner: Historical control data from 13 chronic feeding studies on mice from 1976-80. May be useful information for an oncogenicity study submission. No mouse oncogenicity study is on file.

REPRODUCTION, RAT

No studies submitted; data gap.

TERATOLOGY, RAT

No studies submitted; data gap.

TERATOLOGY, RABBIT

No studies submitted; data gap.

TERATOLOGY, MOUSE

004 959228 (5/23/72, U. Western Ontario) JW, 4/8/85. One liner: Single IP dose of 7, 10, or 14 mg/kg; 3 consecutive doses of 5 mg/kg; or 3 consecutive doses of 10 mg/kg to mice weighing 25-33 grams. The frequency of developmental anomalies in skeletal system, legs, digits, and digestive system was elevated with single doses. No comparisons of individual anomaly type and dose level with corresponding control was statistically significant, but the summations of all anomalies on day 11 were significantly elevated for both 10 mg/kg and 14 mg/kg. There is insufficient information to evaluate the importance of these observations. Reproductive toxicology--depressed fetal weight on or after day 9. Percent of resorptions was not altered in treated groups, but frequency of dead fetuses was increased. Unacceptable study with useful data. Insufficient information on maternal toxicity, protocol, test article, clinical observations, necropsy/histopathology/uterine examination, individual reproductive performance.

MUTATION, GENE

No studies submitted; data gap.

MUTATION, CHROMOSOME

057 040995 (5/2/84, Bayer AG Institute of Toxicology) VVW and BKD, 7/14/86. One liner: Cyclophosphamide was evaluated as a positive control article for the mouse dominant lethal assay. These data may provide useful information for a dominant lethal study submission. No dominant lethal study or other chromosome mutation study is on file.

MUTATION, DNA

No studies submitted; data gap.

NEUROTOXICITY, HEN

008 959218 (Date unknown, Communicable Disease Center, U.S. Dept. of H.E.W.) BKD, 7/16/86. One liner: Demeton delivered by subcutaneous injection in single dose preceded by 15 mg/kg atropine sulfate delivered orally. Doses of 5, 10, 20, 40, 80 mg/kg; four Rhode Island Red hens per dose. Age unspecified; weight 2.5 to 4.0 kg. No muscle weakness or paralysis observed.

008 959242 (1956, F.D.A.) JW, 4/8/85. One liner: Year old chickens fed increasing doses of demeton from 100 to 1600 ppm. Over 18 weeks all birds died with no indications of paralysis or microscopic nerve damage. Since this report is an abstract, its utility is limited.

004 959219 (9/20/66, Farbenfabriken Bayer AG) BKD, 7/18/86. One liner: Demeton was fed to HNL breed hens in doses of 5, 20, 100, or 400 ppm for 30 days. There were 8 hens per group with two killed for histopathology one day after treatment. Observation was for an additional 28 days, followed by killing and histopathology. No muscle or behavioral toxicity observed. Sporadic abnormalities in spinal cord histology were probably not related to treatment (see Record #959221). The high dose group showed reduced feed consumption

and body weights. Four deaths occurred during dosing with 3 in the high dose group and one in the 100 ppm group. Data gap remains. Study unacceptable because no positive control, animals too old, no second dosing period, and test article ill-defined.

004 959221 (7/24/67, Farbenfabriken Bayer AG) BKD, 7/18/86. One liner: This study is the histopathology report for the complete study in Record # 959219.